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09/919,243	07/31/2001	Raghavan Rajagopalan	MRD / 69	2807

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EXAMINER
SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
1644	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
919243	RAJAGOPALAN et al
Examiner	**Group Art Unit**
SAUNDERS	

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P ri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 4/28/03.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-66 is/are pending in the application.

Of the above claim(s) 4-32, 39-66 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-3, 33-38 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Pat nt Drawing Review, PTO-948

☐ Other _____

Office Acti n Summary

The claims pending are 1-66.

Applicant's election with traverse of Group I (claims 1-8 and 33-43 in Paper No. 5 is acknowledged. The traversal is on the ground(s) that all the groups pertain to compounds having the same core structure of an anti-idiotypic (anti ID) antibody (Ab) and a photoactive compound for imaging or therapy and to the uses thereof in therapy or imaging. This is not found persuasive because the examiner does not find that the compounds of the two groups have the same "core structure". The examiner finds that the list of photoactive compounds that serve as imaging dyes (recited in Markush group of claims 1, 11 and 34) differs from that for photoactive compounds that serve as therapeutic agents (recited in the Markush group of claims 16, 28 and 53). Therefore applicant is requesting the examiner to search for two different genuses of compounds without common structure.

As to the separation of the compounds from the methods, this is proper since the compounds have other uses. For example, the anti Id Ab coupled to a dye would be used in a method for immunofluorescent detection of receptors in tissue sections.

Furthermore, applicant's arguments regarding the restriction are self-serving. Applicant has submitted a large disclosure statement with only one relevant reference pertaining to the in vivo use of anti Id Abs as internal image anti-receptor antibodies. This reference is WO 93/00934, which pertains to imaging but not to therapy. If this reference were found to render applicant's imaging compounds or methods obvious, the examiner would not expect applicant to concede that the therapeutic compounds or methods are also obvious.

Since different references would be needed and different rationals would be needed in statements of obviousness for examination of both imaging and therapeutic compounds, applicant is expecting the examiner to carry an undue burden for proper search and examination.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of species such that the anti Id Ab is an anti-steroid receptor internal image Ab, such that the dye is a cyanine, and such that the linker is –HNCONH- is acknowledged. Claims of Group I which read upon the elected combination are 1-2 and 33-36. However, should prior art submitted by applicant or found by the examiner be applicable to any other claims of Group I, these claims will also be examined.

All claims of Group I will be presently examined for informalities.

Claim 41 is objected to because of the following informalities: in claim 41 "CCK receptors" is improper. Applicant should spell out or else enter --(CCK) --after the appropriate receptor in claim 34. Appropriate correction is required.

Claims 33-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 33 recitation of "photodiagnostic composition" is unclear because only one compound of formula I is recited. A "composition" would have more than one compound. What else is in the composition?

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Edelman et al (4,818,684).

Edelman et al teach an anti-Id Ab designated 8 GII-C6 which is secreted by hybridoma HB 8708. This antibody binds a glucocorticoid receptor. See col.9, lines 11-17. This antibody is claimed in a form of being detectably labeled with a fluorescent moiety bound to the antibody (claim 11), which is the same as compound I of claim 33. Any compound with a detectable fluorescent label may be properly considered as a "photodiagnostic composition" since this term would encompass in vitro diagnostic assay materials.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vander-Mallie (4,536,476) in view of Ullman et al (3,996, 345).

This rejection is based upon the fact that the term "photodiagnostic composition" in claim 33 can be properly interpreted as being a composition for in vitro diagnostic methods. In any event, what is claimed in claims, 1 and 3 is simply a compound having formula I, and any intended in vivo use would carry no weight.

Vander-Mallie shows immunoassays in which a labeled anti-Id Ab is used in lieu of a labeled antigen in a fluorescence quenching assay. See col.6, lines 24-28 and example 4. It is noted that the particular embodiment of example 4 utilizes a rhodamine labeled anti-Id Ab. It is also to be noted that Vander-Mallie uses anti-Id Abs which bind to Id –Abs, in the manner of antigen and thus serve as "internal image" mimicks of the antigen. See col.3, lines 35-48 and col.4, lines 22-31. It is to be noted that Vander-Mallie points to Ullman et al (3,996,345) at col.6, lines 24-28. Thus one would have reasonably looked to Ullman et al for direction as to the types of analytes that may be assayed, the types of fluorescent labels that may be used, and the types of linkages between fluorescent labels.

Ullman et al teach numerous analytes ("compounds of interest") starting at col.9, line 26. Note that they teach steroids at col.10, line 22 and cardiotonic glycoids (i.e. a cardiac glycoside") at col.10, line 24. Both of these inherently have receptors. Also every drug of abuse or therapeutic drug listed at col.9, line 41-col.10, line-24 has a receptor. Likewise the peptide and protein hormones listed at col.12, lines 20-49 have receptors.

It is taken that when one followed the direct teachings of Vander-Mallie to in corporate the teachings of Ullman et al one would have necessarily arrived at the instant compound of formula I. Note if one wanted to assay for a steroid, instead of providing a fluorescent label on a steroid analogue, as taught by Ullman et al, one would have, instead, made an idiotypic antibody against the steroid, and then an anti-Id Ab against the idiotypic antibody, as taught by Vander-Mllie. See col.3, line 35-col. 4,

line 49, for example. These are fully analogous to steps that applicant employs at page 11, lines 10-17. Note the steroid analyte of Vander-Mallie/Ullman et al is equivalent to the "ligand" taught by applicant. The anti-Id Ab thus provided for the fluorescence. Quenching assay of a steroid, according to Vander-Mallie/ullman et al would necessarily have the inherent property of binding to a steroid receptor and thus be capable of serving as an "internal image".

As to the fluorescent labels used to label the anti-Id Ab, it is noted that Vander-Mallie used rhodamine. Thus a conjugate using rhodamine would have been reasonably expected to also work in an assay for a steroid. Ullman et al also teaches that numerous other fluorescent labels may be used in a fluorescence quenching immunoassay and one would have had no reason to not expect that these would be coupled to anti-Id Abs. Note col.8, lines 1-35 teaches fluoresceins, rhodamines and various cyanines.

From the above it is clear that claims 33-34 would have been obvious.

Claims 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelman in view of Ullman et al.

Edelman has been cited supra in a 102 rejection of claim 33. Edelman et al do not recite specific fluorescent dyes. Ullman et al teach numerous known fluorescent dyes at col.8, lines 1-35. These include fluoresceine, rhodamines and cyanines. These dyes are taught as being conjugated to antibodies (e.g. examples II and III). Hence the labels recited in instant claim 34 would have been obvious as species of the fluorescent moiety taught by Edelman et al.

Claims 1-3 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vander-Mallie in view of Ullman et al as applied to claims 33-34 above, and further in view of Sterberger.(Immunocytochemistry).

Claims 1-2 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelman et al in view of Ullman et al as applied to claims 33-34 above, and further in view of Sternberger.

Vander-Mallie or Edelman, either in view of Ullman have been cited supra for teaching obviousness of anti-Id Abs that bind to a receptor and that are conjugated to the fluorescent labels recited in claim 34, such as fluorescein and rhodamine. These references do not teach the type of bond formed upon conjugation.

Sternberger (Fig.2-3) is cited for teaching that, when fluorescein or rhodamine isothiocyanate is conjugated to an antibody, a NH-CS-NH linking group is formed. Thus the limitations of claims 1 and 35-36 regarding the linking group would have been obviously obtained upon employing a conventional method of conjugating Rhodamine or fluorescein to the anti-Id Abs of Edelman et al or to those of Vander-Mallie in view of Ullman et al. Further dependent claims reciting specific receptors are rejected in accord with the further above noted teachings of Edelman et al and Vander-Mallie in view of Ullman et al.

Claim 33 is rejected under 35 U.S.C. 102(b) as being entirely anticipated by Rajagobalan (WO 93/00934).

Rajagobalan teaches immunodiagnostic reagents for in vivo imaging. He provide precisely the same motivation as recited instantly for using anti-Id Abs as internal

images to target a receptor (e.g. see para. Spanning pages 2-3 and 4-5). He teaches targeting of glucocorticoid (i.e. steroid) receptors at page 1 and digoxin (i.e. a cardiac glycoside) receptors at page 10. He teaches that the anti-Id Ab may be conjugated to a fluorescent label (page 10, line 8). Thus all features of a compound of formula I are taught.

Claims 1-3 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rajagapolan in view of Ballou et al (cancer Immunol Immunother 41, 257,1995 (ref BT)).

Rajagapolan has been cited supra as anticipating claim 33. Ballou et al teach that cyanine dyes are preferred labels for in vivo imaging. The dyes utilized were supplied as activated N-hydroxy succinimide diesters (page 258, col.1). When conjugated to an anti-Id Ab (or any antibody) these would inherently form the N-succinimido linker recited in claims 1 and 35-36; claims 2-3 and 37-38 are rejected since Rajagopalan has, as noted supra in the 102 rejection, taught these receptors as targets for imaging.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday 8 am - 5:30 pm. and on Alternative Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. The fax phone number

for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Saunders/tgd
August 19, 2003

David A Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644